Remarks

Applicant notes that the previous Amendment submitted inappropriately referred to a foreign document, WO 98/18719, rather than the appropriate corresponding US Patent 6,254,844. This reference was added to describe how to make HAP particles. However, Applicant wishes to again emphatically note that the understanding of how to make HAP particles is not relevant to the present invention. This argument was previously presented in the Amendment of May 1, 2002 on page 5, and has not been considered by the Examiner. Applicant respectfully wishes for the argument set forth on page of the May 1, 2002 be considered and discussed by the Examiner.

Similarly, the Examiner has repeatedly required a Terminal Disclaimer, without acknowledging or dealing with the arguments set forth in the response of May 1, 2002, pages 4 and 5, refuting the terminal disclaimer requirement. Applicant is willing to file a Terminal Disclaimer, if deemed necessary, after the Examiner addresses the arguments set forth in pages 4 and 5 of the May 1, 2002 response.

Applicant notes the Examiner's requirements for changes to the specification set forth on page 9 of the final action (namely, deleting "and curing" and changing the spelling of "chewing gum") and has made those changes to the specification.

A marked-up specification, and substitute specification, are set forth with this RCE. The changes to the specification are set forth using the marked-up version and substitute specification approach, rather than citing specific paragraphs to be changed, because the specification did not previously include paragraph numbers. The substitute specification now includes numbered paragraphs, as well as the appropriate headings.

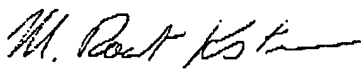
The recitation of Rudin EP '133 against the present invention is inappropriate because Rudin EP 664 133 is from the same inventor as the present application. The enclosed declaration under 35 USC 1.132 is submitted to overcome the rejection of the claims on the basis of Rudin. A declaration under 37 CFR 1.132 is included herewith, on the following page. This Declaration should overcome the rejection of the claims on the basis of Rudin '133.

Response Under 37 CFR 1.116
Expedited Procedure
Examining Group 1614

This Amendment After Final Action is necessary to place the claims in condition for allowance or in better condition for appeal. The Amendment after Final Action is submitted together with an RCE. A request for a three month extension of time in which to respond to the outstanding Office Action is respectfully petitioned for. PTO Form 2038 is enclosed authorizing charging a credit card for the prescribed Small Entity three month extension fee, as well as the appropriate RCE fee. Please charge any ADDITIONAL fees due or credit any refunds to deposit account 11-0665. A duplicate of this page is enclosed for this purpose.

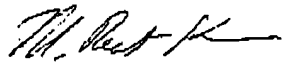
Wherefore, further consideration and allowance of the claims is respectfully petitioned for.

Respectfully submitted,



M. Robert Kestenbaum
Reg. No. 20,430
11011 Bermuda Dunes NE
Albuquerque, NM USA 87111
Telephone (505) 323-0771
Facsimile (505) 323-0865

I hereby certify this correspondence is being submitted to Commissioner for Patents, Alexandria, Va. by facsimile on September 17, 2003, fax number (703) 872-9306.



M. Robert Kestenbaum

STOMATIC COMPOSITION

~~Description~~

~~Field of the Invention~~

Cross-References to Related Applications

Not applicable.

Statement Regarding Federally Sponsored Research or Development

Not applicable.

Background of the Invention

[0001] This invention relates to the field of medicine, and in particular to the field of stomatology and may be used for preventive treatment ~~and curing~~ of carics, parodenitis and paradentosis.

Technical Field

[0002] Industrial application

[0003] The stomatic composition can be used to cure microdefects of the basic substance of the dental enamel, e.g. to prevent the spread of caries, and is also useful for preventive measures avoiding the spread of inflammable-destructive diseases of paradentium tissues, such as pardenitis and paradentosis.

[0004] The stomatic composition can be used in the form of tooth pastes, tooth creams and gels. Moreover, the composition can be included as a component in chewing gum, pastilles, tooth elixir and formulations to rinse mouth.

[0005] The stomatic composition according to the invention is capable to stimulate reparative osteogenesis processes and possessing a high bioactivity and specific pharmacological activity. Moreover, this composition is useful for combatting dental caries and to prevent the spread of such inflammable-destructive diseases of paradentium tissues as paradenitis and paradentosis, on the basis of hydroxyapatite also optionally comprising abrasive materials, humectants, thickeners, surfactants, flavouring agents, and a number of optional ingredients.

~~Prior art~~

[0006] For these above-captioned purposes, stomatic compositions comprising hydroxyapatite (HA) have found an extensive application in the stomatologic practice.

[0007] There are certain compositions having a favourable effect including synthetic HA containing 92 to 97% $Ca_{10}(PO_4)_6(OH)_2$, 3 to 6% H_20 and 0,3% $CaCO_3$ with an average particle size of 1 to 15 ìm.

[0008] Such a stomatic composition, for instance, according to Patent EP 0344832 cl. A61K 7/16, comprises save the stated HA, water-soluble casein material or sodium trimetaphosphate, as an anti-caries agent and also other well known ingredients which depend upon the forms of the product manufactured, such as various humectants, binding thickeners, surfactants, flavouring agents.

[0009] The known stomatic composition (EP 03442746 cl. A61K 7/18, publ.23.11.89) supplementary includes a fluorine-containing compound in the form of NaP or sodium monophluorphosphate as an anti-caries agent.

[0010] The amount of HA present in the stomatic composition is in the range of 1 to 50%, usually 2 to 20% by weight of the stomatic composition. The stomatic composition comprises some other ingredients: humectants, thickeners, surfactants and flavouring agents commonly known to those skilled in the art in all formulations of such products.

[0011] However, the stomatic compositions stated possess a

[0012] relatively poor anti-caries effect and is not useful in the preventive medicine and in the treatment of inflammatory-destructive diseases of paradentium tissues.

~~Disclosure of the invention~~

Summary of the Invention

[0013] It is an object of the present invention to create a stomatic composition comprising compounds capable to cure microdefects of the basic substance of the dental enamel to combat caries developing (e.g. to provide an anti-caries activity) and to prevent the spread of such inflammable-destructive diseases of paradentium tissues as paradenitis and paradentosis, and also compounds capable to stimulate reparative osteogenesis processes and possessing high bioactivity and specific pharmacological activity.

[0014] It is a further object of the invention to create a stomatic composition being identic to the basic substance of the dental enamel in its substance contents and crystalline parameters, as the acid formed in the materials covering dental surfaces causes

destruction of mineral hydroxyapatyte out of which enamel is composed and has a result due to which calcium ion loss occurs.

Detailed Description of the Invention

[0015] The task surprisingly has been solved in a composition ~~as defined in claim 1~~ characterised in that it comprises particles of hydroxyapatite with an average particle size in length (l), width (d) and thickness (h) of: (l) from about 0.2 μm to about 0.01 μm, (d) from about 0.1 μm to about 0.001 μm, and (h) from about 0.1 μm to about 0.0001 μm with the particles of hydroxyapatite having a specific surface of hydroxyapatite from 100 m^2/g to 150 m^2/g..

[0016] A preferred composition having a more pronounced effect in view of the improvements obtained according to the invention comprises particles of hydroxyapatite with an average particle size in length (l), width(d) and thickness(h) of about l = 0,06 ìm +/- 50 %,

[0017] d = 0,015 ìm +/- 50 % and h = 0,005 ìm +/- 50 %.

[0018] A most preferred composition having a surprisingly superior effect in view of the improvements obtained according to the invention comprises particles of hydroxyapatite with an average particle size in length (l), width(d) and thickness(h) of l about 0,06 ìm, d about 0,015 ìm, h about 0,005 ìm.

[0019] Being introduced into the composition, HA possesses osteo-reparative properties and contains preferably about 100% $Ca_{10}(PO_4)_6(OH)_2$.

[0020] The specific surface of HA used in the composite advantageously is 100 to 150 m^2/g.

[0021] ~~Pages 1-3a of~~ US Patent 6,254,855 column 2, line 30 to column 4, line 35 which is based on WO 98/18719 (of the same inventor) are hereby incorporated by reference into the present application. The pages of ~~WO 98/18719~~ US Patent 6,254,855 describe a method for producing a suspension of hydroxyapatite as described in this application.

[0022] The amount of HA present in the oral composition of the present invention is in the range of 0,1% to 50%, preferably from 0,1% to 25%, and most preferably from about 0,2% to 20% by weight of the oral composition.

[0023] The composition reacts to a change in the biochemical environment, for instance a rapid dissolvement of ultra finely divided HA occurs when the pH is decreasing, that provides an active utilization of Ca and PO_4 - ions in the osteogenesis process: the size and configuration of the inventive crystals are adapted to the maximum to the dental enamel structure, which is mostly composed of HA, that suggests its use in the osteo-reparative process as a building material.

[0024] The ultra finely divided HA possesses a high adhesive-sorption activity to the dental enamel and to microdefects on its surface, that favour the preventive measures preventing the spread of caries disease and also possesses a high sorption activity in respect to proteins and aminoacids of paradentium tissues, that stimulates an active preventive treatment of the inflammable-destructive diseases such as paradenitis and paradentosis.

[0025] Moreover, the stomatic composition of the present invention will contain other conventional ingredients in addition to HA possessing osteo-reparative properties, whose introduction into the composition depends on the form of the product. For instance, in the case of an oral product in the form of dentifrice paste, cream or gel, the product will comprise a liquid phase containing humectants and binding thickeners which act to maintain the particulate solid abrasive and HA crystals in the form of stable suspension in the liquid phase.

[0026] Surfactants and flavouring agents are also usual ingredients for various inventive embodiments of oral compositions.

[0027] The humectants usually used are glycerol or sorbitol. However, other humectants may be used according to the invention including polyethyleneglycol, propyleneglycol, lactitol and hydrogenated corn syrop. The amount of humctant will generally range from about 0% to 85% by weight of product. The remainder of the liquid phase will consist substantially of water. The liquid phase can be water or a non-aqueous composition.

[0028] As binding agents and thickeners, various substances can be used such as sodium carboxymethylcellulose, sodium hydroxyethylcellulose and xanthan gum. Natural gum bindings can be included such as gum tragacanth, gum karaya of Irish moss, etc. Any mixture of binding agents and thickeners can be also used. The amount of bindings

and thickeners usually included into the oral composition is in the range of 0% to 10% by weight of the oral composition.

[0029] Moreover, any materials as widely disclosed in the literature generally also might be used for the invention as surfactants, i.e. surfactants like sodium lauryl sulphate, dodecylbenzene sulphonate and sodium lauryl sarcosinate. Other anionic surfactants also can be used as well as cationic and amphoteric and non-ionic surfactants. Surfactants are generally present in the composition in the amount of 0% to 5% by weight of the oral composition.

[0030] Flavours that are generally used in the oral compositions are those based on oils of spearmint and peppermint and might be used for the invention. Examples of other flavouring materials used are menthol, clove, wintergreen, eucalyptus and aniseed. A preferable amount of flavours is from 0% to 5% by weight in respect to the oral composition.

[0031] As abrasive materials, silica dioxide of various modifications, aluminium oxide, calcium carbonate, dicalcium phosphate anhydrite, dicalcium phosphate dihydrate, sodium metaphosphate insoluble in water, and thereof mixtures may be used. The amount of abrasive materials ranges from 0.0% to 25%. The oral composition may include a wide variety of optional ingredients. These include antimicrobial and anti-plaque agents for example chlorhexidine or 2,4,4-trichloro-2hydroxy-diphenyl ether, or zink compounds (see EPA-161898) anti-tartar ingredients such as condensed phosphates, e.g. alkali et al pyrophosphates, hexametaphosphatesor polyphosphates (see US-A-4 515772 and US-A-4 627977) or zinc citrates (see US-A-4 100269), sweetening agents such as saccharin. Preservatives such as formalin, sodium benzoate. colouring agents (for instance titanium dioxide) or pH-controlling agents, such as acid base or buffer agents the oral composition may also include agents enhancing the gingivitis system of the mouth cavity and representing extracts of various natural plants such as urtica, millefolium, chamomilla hypericum, salvia, etc. in the aqueous or aqueous-alcoholic forms.

[0032] The stomatic composition depending on its form (dentifrice paste, cream or gel) is maintained in contact with the tissue of the oral cavity from 15 sec to 12 hours.

[0033] The following examples of dentifrice pastes and gel comprising synthetic ultra finely divided HA possessing osteo-reparative properties as described above illustrate the invention. Percentages and parts of the components are by weight.

[0034] Below-standing preferred embodiments of the invention are shown in its composition.

Examples N1 and 2.

Toothpaste prepared from the following ingredients.

	Ingredients,%	
Example	1	2
Ultra finely divided Hydroxyapatite	0,2	2,0
Silica aerogel	22,0	15,0
Sodium carboxymethylcellulose	1,0	1,0
Glycerol distilled	20,0	20,0
Sorbitol	20,0	17,0
Titanium dioxide	0,6	0,5
Sodium benzoate	0,4	0,6
Aqueous-alcohol extract of chamomilla	1,0	0,8
Aqueous-alcohol extract of hypericum	1,0	0,8
Sodium saccharin	0,1	0,06
Flavour	1,0	1,3
Sodium lauryl sulphate	1,5	1,5
Water	to 100,0	to 100,0

Examples N 3 to 7

Toothpaste prepared from the following ingredients.

	Ingredients,%				
Example	3	4	5	6	7
Ultra finely divided hydroxyapatite	2,5	2,5	2,5	2,5	2,5
Silica aerogel	17,0	17,0	17,0	17,0	17,0
Sodium hydroxyethylcellulose	1,6	---	---	1,6	---
Sodium carboxymethylcellulose	---	1,1	1,1	---	0,9
Sorbitol	20,0	20,0	16,0	20,0	20,0
Glycerol distilled	20,0	20,0	20,0	20,0	20,0
Polyethyleneglycol	---	---	5,0	---	---
Sodium lauryl sulphate	1,5	1,5	1,5	1,5	1,5
Tetrasodium pyrophosphate	---	1,5	---	---	---
Tetrapotassium pyrophosphate	---	---	---	2,5	---
Sodium trimetaphosphate	---	---	2,0	---	---
Zinc citrate trihydrate	---	---	---	---	0,5
Titanium dioxide	0,6	0,6	0,6	0,6	0,6
Sodium benzoate	0,5	0,5	0,6	---	---
Formalin	---	---	---	0,05	0,05
Aqueous-alcohol extract of salvia	0,5	0,5	---	---	---
Aqueous-alcohol extract of millefolium	0,9	0,9	0,5	0,5	---
Aqueous-alcohol extract of chamomilla	---	---	1,0	0,7	---
Triclosan	---	---	0,2	---	0,2
Sodium saccharin	0,06	0,06	0,06	0,06	0,06
Flavour	1,0	1,0	1,0	1,0	1,0

Water (in all examples) to 100,0

Examples N8 and 9

Gel preventing paradenitis.

	Ingredients,%	
Example	8	9
Ultra finely divided hydroxyapatite	5,0	4,0
Sodium hydroxyethylcellulose	2,0	2,5
Silica aero	5,0	---
Glycerol distilled	10,0	---
Sorbitol	25,0	45,0
Sodium benzoate	0,5	---
Triclosan	---	0,3
Flavour	0,2	0,15
Sodium lauryl sulphate	0,2	0,15
Sodium saccharin	0,07	0,07
Water	to 100,00	to 100,00

Industrial application

[0035] The stomatic composition can be used to cure microdefects of the basic substance of the dental enamel, e.g. to prevent the spread of caries, and is also useful for preventive measures avoiding the spread of inflammable destructive diseases of paradontium tissues, such as pardenitis and paradentosis.

[0036] The stomatic composition can be used in the form of tooth pastes, tooth creams and gels. Moreover, the composition can be included as a component in jewing gum, pastilles, tooth elixir and formulations to rinse mouth.

[0037] The stomatic composition according to the invention is capable to stimulate reparative osteogenesis processes and possessing a high bioactivity and specific pharmacological activity. Moreover, this composition is useful for combatting dental caries and to prevent the spread of such inflammable destructive diseases of paradentium tissues as paradenitis and paradentosis, on the basis of hydroxyapatite also optionally comprising abrasive materials, humectants, thickeners, surfactants, flavouring agents, and a number of optional ingredients.

Abstract of the Disclosure

A stomatic composition has particles of hydroxyapatite with an average particle size in length (l), width (d) and thickness (h) of: l from 0.2 μm to about 0.01 μm, d from about 0.1 μm to about 0.001μm, and h from about 0.1 μm to about 0.001 μm.